REMARKS

Applicants request reconsideration of this application in view of the following remarks.

Claims 69-84 are currently pending in this application, with claims 69, 73, 76, 79, 80 and 81 being independent. Claims 1-68 have been cancelled previously without prejudice to or disclaimer of the subject matter recited therein.

At the outset, Applicants would like to thank the Examiner for withdrawing the obviousness-type double patenting rejection and the obviousness rejection previously set forth in the prior Office Action dated September 27, 2004.

In the Office Action dated June 16, 2005, claims 69-84 have now been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Specifically, the Office Action focuses on the use of the term "about" in the claims and suggests that the term "invites subjective interpretations" and that "the public would not be informed of the boundaries of what constitutes infringement of the present claims." Moreover, claims 69-84 have been rejected under 35 U.S.C § 102(e) as being anticipated by U.S. Patent No. 6,100,274 to Kou.

Turning first to the rejection in the Office Action pursuant to 35 U.S.C. § 112, second paragraph, Applicants traverse this rejection and respectfully submit that, contrary to the assertions set forth in the Office Action, the term "about" in the claims by no means renders them indefinite.

As we have indicated previously, the term "about" in the independent claims is used by Applicants to include that range of values (i.e., 80%-125% of the recited value) that is considered to be bioequivalent for a systematically absorbed formulation, as understood by a person having ordinary skill in the art. (*See* 21 C.F.R. § 320.1 for a definition of "bioequivalence." *See also, e.g.,* Food and Drug Administration, Guidance for Industry – Bioavailability and Bioequivalence Studies for Orally Administered Drug Products – General Considerations (March 2003) at p. 20 for a discussion of the 80%-125% bioequivalent range of values.) It is appropriate for the claims to recite such a range since each of the independent claims focuses on achieving a steady state plasma concentration of desloratadine at or after a certain time of administration of the drug.

More specifically, a review of the pending independent claims reveals that each such claim requires achieving an arithmetic or geometric mean steady state maximum plasma concentration (C_{max}) of desloratadine of about 4 ng/mL, and an arithmetic or geometric mean time to maximum plasma concentration (T_{max}) of desloratadine of about 3 hours post dose. Applicants believe that this is a specific and definite limitation that clearly delineates the metes and bounds of Applicants' invention, as claimed in the pending independent claims. Accordingly, use of the term "about" does not render the claims 69-84 indefinite, and Applicants therefore request that the rejection under 35 U.S.C. § 112, second paragraph be withdrawn.

Applicants also respectfully traverse the rejection of the pending claims pursuant to 35 U.S.C § 102(e) in view of the Kou patent. The Kou patent teaches stable pharmaceutical compositions comprising 8-chloro-6-11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cycloheptic[1,2-b]pyridine (also referred to as "DCL," "descarbonylethoxyloratadine" and "desloratadine"), a DCL protective amount of a pharmaceutically acceptable basic salt such as calcium dibasic phosphate, and an amount of at least one disintegrant. Column 5, lines 44-54 of Kou states that "the anti-allergic effective amount of descarbonylethoxyloratadine for oral administration" is preferably about 5 to 10 mg/day in single or divided doses, and most preferably 5 mg, once a day. Column 5, lines 49-56 specifically states:

> Of course the precise dosage and dosage regimen may be varied depending upon the requirements of the patients (e.g., his or her sex, age) as well as the severity of the allergic condition being treated. Determination of the proper dosage and dosage regimen for a particular patient will be within the skill of the attending clinician.
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> Descarbonylethoxyloratadine possess *(sic)* antihistaminic properties.

The Office Action indicates that the pending claims are inherently anticipated by the Kou patent because identical dosages are disclosed (i.e., 5 mg/day) and because "one of ordinary skill in the art is able to readily envisage about 10 days of treatment from the disclosure of Kou" (emphasis added).

Applicants respectfully submit that this rejection should be withdrawn, because the Office Action applies the incorrect standard for inherent anticipation. As the Federal Circuit confirmed in Continental Can Co. v. Monsanto Co., 948 F.2d 1264 (Fed. Cir. 1991), "[i]nherency ... may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not the test." The proper test for inherent anticipation is whether the claimed invention "necessarily results from" the disclosure in the allegedly inherently anticipating reference. (*See, e.g.,* Rapoport v. Dement, 254 F.3d 1053, 1062-63 (Fed. Cir. 2001), and Schering Corp. v. Geneva Pharmaceutials, Inc., 339 F.3d 1373, 1381 (Fed. Cir. 2003).) Therefore, it is not sufficient that one might "readily envisage" Applicants' claimed invention, as suggested by the Office Action. *See also* MPEP ¶ 2112, part IV.

In the Rapoport case, the Federal Circuit found that, in challenging the validity of a claim based on inherent anticipation, Rapoport failed to meet the applicable evidentiary standard, since it failed to offer positive evidence that the prior art necessarily results in the method of the treatment contemplated in the patent. Indeed, the Federal Circuit held that Rapoport failed to foreclose the possibility that other factors were needed to combine with the prior art in order to reach the claimed invention. *See also* Toro Co. v. Deere & Co., 355 F.3d 1313, 1314 (Fed. Cir. 2004) (no inherent anticipation if outside factors are capable of intervening between the prior art and the challenged invention).

Applicants submit that the Office Action does not show that Applicants' claimed invention "necessarily results from" the disclosure in the Kou patent. The targeted pharmacokinetic profile in each of the independent claims does not "necessarily result" from the disclosure in the Kou patent. The Kou patent does not discuss how to administer desloratadine in order to achieve an arithmetic or geometric mean steady state maximum plasma concentration (C_{max}) of desloratadine of about 4 ng/mL, or to achieve an arithmetic or geometric mean time to maximum plasma concentration (T_{max}) of desloratadine of about 3 hours post dose. Nor does the Kou patent discuss the factors that might be changed to achieve this aspect of Applicants' claimed invention. For example, the Kou patent does not disclose or suggest the pK

profile that would result from administering a single desloratadine tablet. Nor does the Kou patent discuss the number of days for which it is necessary to administer desloratadine to achieve a steady state, as specifically contemplated in claim 73. Indeed, the Kou patent teaches that the precise dosage and dosage regimen can be modified depending on the requirements of the patients as well as the severity of the allergic condition being treated. Kou patent, col. 5, lines 49-52. There is no disclosure or suggestion of a target desloratadine pK profile in Kou, much less a steady state target pK profile.

Morever, it is apparent upon reviewing the disclosure in U.S. Patent Appln. Pub. No. US 2003/0004179 to Affrime et al. that the pK profile is variable and can be affected by outside factors. For example, the Affrime et al. published application teaches at p. 2 that either one 5 mg desloratadine tablet or one 10 mL dose of desloratadine syrup (0.5 mg/mL) was administered to certain adult patients under fasting conditions, and reports a resulting mean C_{max} of 2.19 ng/mL in Tables 1 and 2 from these administrations. This C_{max} value is only slightly more than half of the arithmetic or geometric mean steady state maximum plasma concentration (C_{max}) value of about 4 ng/mL claimed by Applicants and is well outside of the 80%-125% range of this value claimed by Applicants. A copy of the Affrime et al. published application is attached, and also submitted under cover of a Second Supplemental Information Disclosure Statement for the Examiner's consideration.

Accordingly, the disclosure of the Kou patent does not necessarily result in the invention claimed in the present application, and therefore does not inherently anticipate that claimed invention.

Applicants submit each of the currently pending claims in this application has overcome the presently outstanding rejections and are allowable. Applicants also believe that the dependent claims are allowable, in their own right, for defining other patentable features of the present invention in addition to those recited in their respective independent claims. Accordingly, the Examiner is respectfully requested to pass this application to issue.

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Respectfully submitted,

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